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EXAMINER	
BORIN, MICHAEL L	
ART UNIT	**PAPER NUMBER**
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/691,012	BUCHARDT ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/108,591.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/09/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 34-73 are pending .

Response to restriction requirement filed 06/20/2007 is acknowledged. Applicant's traversal is considered and is deemed persuasive. The restriction requirement is hereby vacated.

2. It is noted that Applicants have copied claims 1, 2, 5, 10, 16-19, 24, 32-34, 43 and 52 of U.S. Patent No. 6,472,209, issued on October 29, 2002. The remaining pending claims are at least directed to substantially the same subject matter as claims that issued in U.S. Patent No. 6,472,209.

Information Disclosure Statement

3. Applicants' Information Disclosure Statement filed 02/09/2004 has been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

Sequence Listing

4. The Sequence Listing was approved by STIC for matters of form.

Claim Objections

5. Claims 46, 47 are objected to because of the following informalities: The claims are duplicates. Appropriate correction is required.

Claim Rejections - 35 USC § 112(New Matter)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 35,37, 41-47,49, 55,58-60, 63,66,73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The following claims, copied from claims of U.S. Patent No. 6,472,209, do not have sufficient written description :

- claims 35,41-47,49,58-64,66 directed, in part, to a step of detecting of biological response
- claims 37,42 directed to polypeptide participating in cell signaling

- claims 40,45,55,63, directed to biological response characterized by physiological changes

Priority

7. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). The disclosures of the prior-filed applications, Application Nos. 08/108591 and 10/154890, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. As stated in rejection under 35 U.S.C. 112, first paragraph, above, claims 35,37, 41-47,49, 55,58-60, 63,66,73 do not have sufficient description as follows:

- claims 35,41-47,49,58-64,66 directed, in part, to a step of detecting of biological response

- claims 37,42, directed to polypeptide participating in cell signaling
- claims 40,45,55,63, directed to biological response characterized by physiological changes

Accordingly, claims 35,37, 41-47,49, 55,58-60, 63,66,73 are not entitled to the benefit of the prior applications.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 37, 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is applied for the following reasons.

Claims 37,42 lack antecedent basis as they address "said polypeptide" – there is no "polypeptide" addressed in the correspondent base claim

Claim Rejections - 35 USC § 102 and 103.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9. Claims 34,48,57,65,73 are rejected under 35 U.S.C. 102(e) as anticipated by Summerton et al (US 5,142,047)

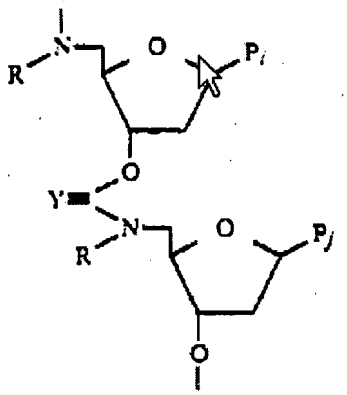
The instant claims are drawn to method of treating by *in vivo* administration of a polyamide nucleic acid oligomer containing neutral amide backbone linkages which is complementary to a target nucleic acid, under conditions wherein said oligomer engenders a biological response associated with said target. The claims specify that the administration is "extracellular". Claims 34-47 are directed to method of "treating living cells", whereas methods of claims 48-73 are addressed as methods "comprising administering" said oligomer. Further, claims are directed to treating either cells, or mammals or organism (claims 34-40,48-57, claims 41-47, 58-64, and claims 65-73, respectively).

As the claims are directed either to extracellular administering *in vivo* or to treatment comprised of administering *in vivo*, it is Examiner's position that any reference teaching *in vivo* administration of oligomer as claimed will read on "extracellular administering *in vivo" or on* "treatment comprised of administering *in vivo*". As for the limitation "administering under conditions wherein said oligomer engenders a biological response associated with said target", again, it is Examiner's position that any reference

teaching *in vivo* administration of oligomer as claimed (i.e., oligomer which is complementary to a target nucleic acid) is read as administering under conditions wherein said oligomer engenders a biological response associated with target nucleic acid to which the applied oligomer is complementary.

As such the following references are considered to read on the invention as claimed.

Summerton et al (US 5,142,047)[1] teach therapeutic administration of compounds such as compound of formula B-B (col. 5):



wherein, for Y=O, the compound is an "oligomer containing neutral amide backbone linkages". Further, as compounds to be administered are binding compounds having desired binding activity to selected target sequence (col. 5, lines 1-7, and col. 16, bottom), and a target sequence is a single-stranded polynucleotide (col. 4, bottom) the oligomers of 5,142,047 read on oligomers administered per the instant invention. which is complementary to a target nucleic acid

[1] Exemplary reference of multiple patents of the same applicant

It is the Examiners position that all the elements of Applicant's invention with respect to the specified claims are instantly disclosed by the teaching of the reference cited above

10. Claims 34,36,38,39,48,50-54,56,65,67-72 are rejected 35 U.S.C.103(a) as obvious over Summerton et al (US 5,142,047).

The reference is applied as above. Summerton et al does not teach such limitations as administering to a mammal in particular (as in claims 36,48,67), administering via intraperitoneal route (as in claims 46,47,56,64,72), and addressing nature of polypeptide (as in claims 52,60,69) and effect thereon (as in claims 38,39,53,54,61,71).

With respect to the above claims 34,36,38,39,48,50-54,56,65,67-72, if there are any differences between Applicant's claimed method and that of the prior art, the differences would be appear minor in nature. Although the prior art do not teach the nature of the target organism, way of administering, and addressing nature of polypeptide, it would be conventional and within the skill of the art to select and/or determine such conditions as their selection for the intended purpose of *in vivo* treatment is well known in the art; and selecting and/or determining such conditions is conventional and within the skill in the art to which this invention pertains.

11. Claims 35,37, 41-47,49, 55,58-60, 63,66,73 are rejected under 35 U.S.C. 102(e) as anticipated by Richelson et al (US 6,472,209)

The claims addressed herein are denied benefit of the filing dates of prior applications and are therefore, subject of rejection over intervening prior art, Richelson et al (US 6,472,209).

Claims 35,41-47,49,58-64,66 directed, in part, to a step of detecting of biological response are anticipated by claims 2 of Richelson et al

Claims 37,42 directed to polypeptide participating in cell signaling are anticipated by claims 7,10 of Richelson et al

Claims 40,45,55,63, directed to biological response characterized by physiological changes are anticipated by claim 18 of Richelson et al.

Claim Rejections - 35 USC § 112, first paragraph (eneblement).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 34-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* treatment, does not reasonably provide enablement for *in vivo* extracellular administration of a representative of genus of a "polyamide nucleic acid oligomer containing neutral amide backbone linkages which is complementary to a target nucleic acid" to produce an [unspecified] biological response.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Specification describes inhibition of transcription by PNA *in vitro* (Example 68), and inhibition of expression of E2 mRNA of papillomavirus *in vitro.* There are no examples of *in vivo administration as claimed and of* effect thereof.

The assertion of the alleged *in vivo* effect stems from observation that the oligomers used in the method

...are able to recognize duplex DNA by displacing one strand, thereby presumably generating a double helix with the other one. Reagents which recognize 17-18 bases are of particular interest since this is the length of unique sequences in the human genome. The compounds of the invention also should be able to form triple helices with dsDNA.

Whereas the improved binding of the compounds of the invention should render them efficient as antisense agents, it is expected that an extended range of related reagents may cause strand displacement, now that this surprising and unexpected new behavior of dsDNA has been discovered. Paragraphs [0056]-[0057]

Based on this alleged (emphasis added in the quotation above) effect, specification states that the method is applicable to *in vivo* treatment:

[0058] Thus, in one aspect, the present invention provides methods for inhibiting the expression of particular genes in the cells of an organism, comprising administering to said organism a reagent as defined above which binds specifically to sequences of said genes.

[0059] Further, the invention provides methods for inhibiting transcription and/or replication of particular genes or for inducing degradation of particular regions of double stranded DNA in cells of an organism by administering to said organism a reagent as defined above.

However, there is no demonstration that PNAs administered in vivo will be capable to exert the same as observed in vitro and in cell-free environment. Neither there is a guidance of the dosages and regimes that would enable PNAs to get across

cell membranes under in vivo conditions and exert their effect on the complementary nucleic acids.

Contrary, Ganesh et al. (review, one of the author of which, P. Nielsen, is applicant of this invention) teach that although peptide nucleic acids are known since beginning of 90-s (i.e., time of filing the priority application of this application),

> some, but surely not all, of the promises expected from this molecule has materialized. Most success, has been achieved within diagnostic use of PNA oligomers in hybridization and PCR. The development of PNA oligomers into gene therapeutic drugs is still in its infancy. (p. 931)

Ganesh et al acknowledge that progress in the use PNAs as therapeutic drugs - in particular concerning cellular delivery - has been made within the past couple of years (and refers to publications of years 1999-2000)

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art at the time the invention was made could not make and/or use the invention with the claimed breadth without an undue amount of experimentation. The skilled practitioner would first turn to the instant specification for guidance in practicing the full scope of the claimed method, however the specification only provides guidance to limited *in* vitro applications.. As such the practitioner would turn to the prior art for such guidance, however the prior art, at the time the invention was made, also lacked knowledge on how to produce *in vivo* effect on intracellular nucleic acid targets by extracellular administering PNAs. Finally, said practitioner would turn to trial and error experimentation to discover conditions of an *in* vivo administration without guidance from the specification or the prior art. Such represents undue experimentation.

Further, with respect to claims 38,43,53,61,70 drawn to "modification" of polypeptide expression, while specification provides support for inhibition of protein expression, it does not provide support for any other modification (e.g., stimulation) of polypeptide expression.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael Borin, Ph.D.
Primary Examiner
Art Unit 1631

mlb